Breakout Session 2
Validation of Safety and Efficacy Biomarkers

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Content

- **Scope**
- **Process map**
- **Profile of an ideal BM**
- **The path from exploratory to known valid BM**
- **Elements of BM validation**
- **Who should be be involved**
- **Should we have different process maps for different types of BMs?**
- **Consensus**
- **Challenges when bridging into clinics**

Scope

- Discuss process maps for the validation of genomics biomarkers of safety and efficacy
- Refer to specific examples for genomic biomarker validation
- Reach a consensus on a revised version of these process maps

… and efficacy? Is a clinical case study beeing added?

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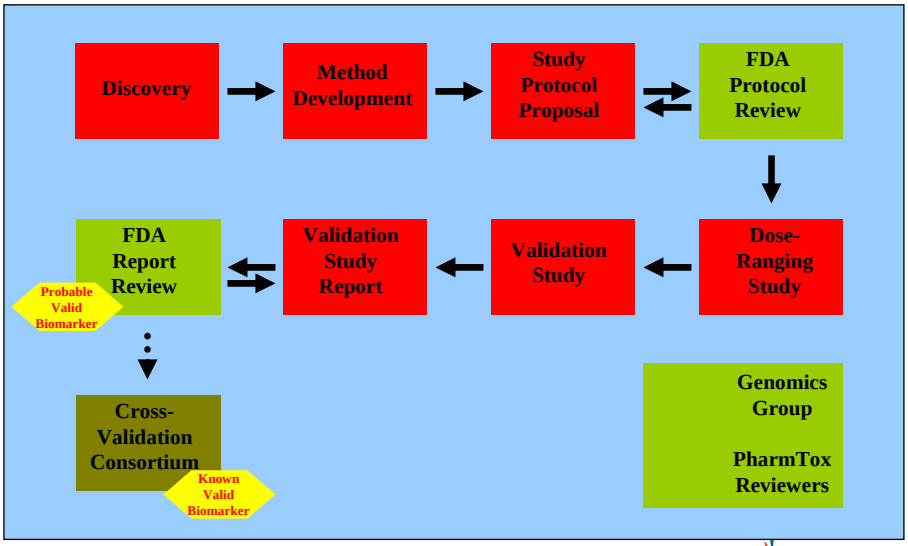
Baseline Process Map for Biomarkers of Preclinical Drug Safety Assessment



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What is the profile of an ideal BM?

- Early
- Sensitive
- Specific
- Predictive
- Reproducible
- Robust
- Accurate/precise
- Accessible Sample
- Inexpensive
- Biologically/ mechanistically relevant
- Superior to existing markers
- Other?

The path from exploratory to known valid BM:

What are the elements of BM validation?

- **Technical/Assay**
  - **Intra- and inter-sample**
  - **Intra-and inter-laboratory**
  - **Technical validation of assay**
  - **Statistical validation plan**
  - **Mapping to gold standard**
  - **Other?**
- **Biological model**
  - **Intra- and inter-species**
  - **Demonstration of desired profile**
  - **Biochemical, mechanistic relevance**
  - **Other?**

Who should be be involved in the validation and acceptance of BMs?

- **Exploratory BMs**
- **Probable valid BMs**
- **Known valid BMs**

What is needed for regulatory acceptance of a BM?

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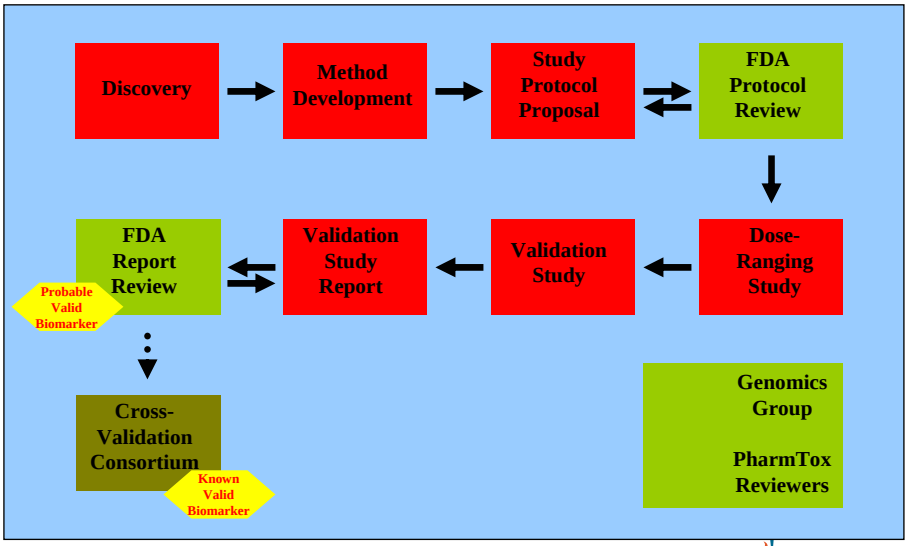
Can we reach a consensus about the process map for biomarker validation?: *a figure ungrouped.*



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What challenges do we face when bridging BMs derived from preclinical experiments are applied in the clinic?

Animals

- Healthy animals models
- Animal disease models
- Target organs easily accessible
- Limited predictivity for humans
  - Potentially different mechanisms
  - Difficulty in making quantitative predictions about toxic effects
  - Verbal feedback not possible
  - Other?

- **Human**
  - Variability in available population of healthy volunteers
    - Lifestyle
    - Co-medication
    - Predisposition for disease
  - Variability in available patient population
    - Lifestyle
    - Co-medication
    - Predisposition for disease
    - State of disease
  - Peripheral tissues accessible
  - Diseases or disease subtypes may be poorly characterized
  - Verbal feedback possible
  - Patient privacy
  - Other?